

We claim:

1. A solid oral controlled-release oral dosage form, the dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration to a human patient, providing a C_{12}/C_{\max} ratio of 0.55 to 0.85, said dosage form providing a therapeutic effect for at least about 12 hours.
2. The dosage form of claim 1 wherein said hydrocodone is dispersed in a matrix comprising said controlled release material.
3. The dosage form of claim 2 wherein said matrix is in multiparticulate form.
4. The dosage form of claim 3 wherein said multiparticulates are compressed into a tablet.
5. The dosage form of claim 3 wherein said multiparticulates are disposed in a pharmaceutically acceptable capsule.
6. The dosage form of claim 1 which provides a C_{12}/C_{\max} ratio of 0.65 to 0.75.
7. The dosage form of claim 1 which provides an in-vitro release of from 18% to about 42.5% by weight of the hydrocodone or salt thereof from the dosage form at one hour when measured by the USP Basket Method at 100 rpm in 700 ml of Simulated Gastric Fluid (SGF) for 55 minutes at 37°C and thereafter switching to 900 ml of Simulated Intestinal Fluid (SIF) at 37°C.
8. The dosage form of claim 6 which provides an in-vitro release of from 18% to about 42.5% by weight of the hydrocodone or salt thereof from the dosage form at one hour when measured by the USP Basket Method at 100 rpm in 700 ml of Simulated Gastric Fluid (SGF) for 55 minutes at 37°C and thereafter switching to 900 ml of Simulated Intestinal Fluid (SIF) at 37°C.

9. The dosage form of claim 1, which provides a dissolution rate in-vitro of the hydrocodone dosage form when measured by the USP Basket method at 100rpm in 900 ml aqueous buffer at a pH of 1.2 at 37°C from about 25 to about 65% by weight hydrocodone or salt thereof released after 2 hours, from about 45 to about 85% by weight hydrocodone or salt thereof released after 4 hours, and greater than about 60% by weight hydrocodone or salt thereof released after 8 hours.
10. The dosage form of claim 1, which provides a dissolution rate in-vitro of the hydrocodone dosage form when measured by the USP Basket method at 100rpm in 900 ml aqueous buffer at a pH of 7.5 at 37°C from about 25 to about 65% by weight hydrocodone or salt thereof released after 2 hours, from about 45 to about 85% by weight hydrocodone or salt thereof released after 4 hours, and greater than about 60% by weight hydrocodone or salt thereof released after 8 hours.
11. The dosage form of claim 1, which provides a T_{\max} of hydrocodone in said patient at from about 2 to about 8 hours after oral administration of the dosage form.
12. The dosage form of claim 1, which provides a T_{\max} of hydrocodone in said patient at from about 3 to about 7 hours after oral administration of the dosage form.
13. The dosage form of claim 1, which provides a T_{\max} of hydrocodone in said patient at from about 4 to about 6 hours after oral administration of the dosage form.
14. The dosage form of claim 1, provides a plasma concentration of hydrocodone of at least 8 ng/ml at from about 2 to about 8 hours after administration and provides a plasma plasma concentration of hydrocodone of at least 6 ng/ml at about 12 hours after administration, based on oral administration of a dosage form containing 15 mg hydrocodone bitartrate.
15. The dosage form of claim 14, which provides a plasma plasma concentration of hydrocodone of at least 8 ng/ml at from about 3 to about 7 hours after administration.

16. The dosage form of claim 1 which provides a C_{\max} of hydrocodone which is less than 50% of the C_{\max} of an equivalent dose of an immediate release hydrocodone reference formulation.
17. The dosage form of claim 1 which provides a C_{\max} of hydrocodone which is less than 40% of the C_{\max} of an equivalent dose of an immediate release hydrocodone reference formulation.
18. The dosage form of claim 1 wherein the dosage form provides a time to 80% mean C_{\max} which is about 90% to about 110% of the time to 80% mean C_{\max} of an equivalent dose of an immediate release hydrocodone reference formulation.
19. The dosage form of claim 1 which provides a time to 80% mean C_{\max} of hydrocodone from about .5 to about 1.5 hours.
20. The dosage form of claim 1 wherein the dosage form provides a time to 90% mean C_{\max} which is about 150% to about 250% of the time to 90% C_{\max} of an equivalent dose of immediate release hydrocodone reference formulation.
21. The dosage form of claim 1 which provides a time to 90% mean C_{\max} of hydrocodone from of about 1.5 to about 2.5 hours.
22. The dosage form of claim 1 which provides a time to 90% mean C_{\max} of hydrocodone from about 1.8 to about 2.2 hours.
23. The dosage form of claim 1 which maintains a plasma concentration within 80% of C_{\max} for about 1 to about 9 hours during the 12 hour dosing interval.
24. The dosage form of claim 1 which maintains a plasma concentration within 80% of C_{\max} for about 4 to about 8 hours during the 12 hour dosing interval.
25. The dosage form of claim 1 which maintains a plasma concentration within 90% of C_{\max} for about 1 to about 6.5 hours during the 12 hour dosing interval.

26. The dosage form of claim 1 which maintains a plasma concentration within 90% of C_{max} for about 2 to about 5 hours during the 12 hour dosing interval.
27. The dosage form of claim 1 which provides a T_{max} at a time point 3 to 4 times later than the T_{max} provided by an equivalent dose of an immediate release hydrocodone reference formulation.
28. The dosage form of claim 1, provides a mean in-vivo absorption rate from administration to T_{max} from about 1.5 mg/hour to about 5 mg/hour and provides a mean rate of absorption from T_{max} to the end of the dosing interval which is less than about 0.5 mg/hour based on oral administration of a dosage form containing 15 mg hydrocodone bitartrate.
29. The dosage form of claim 28 which provides a mean in-vivo absorption rate from administration to T_{max} from about 2 mg/hour to about 4 mg/hour.
30. The dosage form of claim 28 which provides a mean in-vivo absorption rate T_{max} to the end of the 12 hour dosing interval which is from about 0.08 mg/hour to about 0.4 mg/hour.
31. A solid oral controlled-release oral dosage form, the dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration to a human patient, providing a rate of absorption during the time period from T_{max} to about 12 hours after oral administration of the dosage form which is from about 55% to about 85% of the rate of elimination during the same time period, said dosage form providing a therapeutic effect for at least about 12 hours.
32. A solid oral controlled-release oral dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof together with controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration to a patient population, providing a T_{max} of hydrocodone in-vivo at from about 2 to about 8 hours, and providing a

C_{12}/C_{\max} ratio of 0.55 to 0.85, said dosage form providing a therapeutic effect for at least about 12 hours.

33.

A solid oral controlled-release oral dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof together controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration providing a C_{\max} of hydrocodone which is less than about 50% of the C_{\max} of an equivalent dose of an immediate release hydrocodone reference formulation, said dosage form providing a therapeutic effect for at least 12 hours.

34.

A solid oral controlled-release oral dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration providing a time to 80% mean C_{\max} which is about 90% to about 110% of the time to 80% mean C_{\max} of an equivalent dose of an immediate release hydrocodone reference formulation, said dosage form providing a therapeutic effect for at least 12 hours.

35.

A solid oral controlled-release oral dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof and controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration provides a mean in-vivo absorption rate from the time of oral administration to a human patient to T_{\max} of about 2 mg/hour to about 4 mg/hour and which provides a mean in-vivo absorption rate from T_{\max} to about 12 hours after administration which is from about 0.08 mg/hour to about 0.4 mg/hour, said dosage form providing a therapeutic effect for at least 12 hours, based on oral administration of a dosage form containing 15 mg hydrocodone bitartrate.

36.

A method of providing effective analgesia in a human patient for at least about 12 hours comprising orally administering a dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material

to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form providing after a first administration to a human patient a C_{12}/C_{\max} ratio of 0.55 to 0.85 and a therapeutic effect for at least about 12 hours.

37. A process for the preparation of a solid oral controlled-release oral dosage, comprising incorporating an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, into controlled release material to make a dosage form suitable for twice-a-day administration to a human patient, wherein said dosage form after a first administration to a human patient provides a C_{12}/C_{\max} ratio of 0.55 to 0.85 and a therapeutic effect for at least about 12 hours.

38. A solid oral controlled-release oral dosage form, the dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form after a first administration to a patient population, providing a mean C_{12}/C_{\max} ratio of 0.55 to 0.85, said dosage form providing a therapeutic effect for at least about 12 hours.

39. A solid oral controlled-release oral dosage form, the dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form providing an in-vitro release of at least 18% to about 42.5% by weight of the hydrocodone or salt thereof from the dosage form at one hour when measured by the USP Basket Method at 100 rpm in 700 ml of Simulated Gastric Fluid (SGF) for 55 minutes at 37°C and thereafter switching to 900 ml of Simulated Intestinal Fluid (SIF) at 37°C.

40. A solid oral controlled-release oral dosage form, the dosage form comprising an analgesically effective amount of hydrocodone or a pharmaceutically acceptable salt thereof, and controlled release material to render said dosage form suitable for twice-a-day administration to a human patient, said dosage form providing a dissolution rate in-vitro of

passed after 8 hours

- salt thereof released after 8 hours
 d-release oral dosage form, the
 amount of hydrocodone or a pharmaceutically acceptable salt thereof in the dosage form is sufficient to render said dosage form non-toxic to a patient, said dosage form providing a therapeutic effect when measured by the amount of hydrocodone or a pharmaceutically acceptable salt thereof released after 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 12 hours, 14 hours, 16 hours, 18 hours, 20 hours, 22 hours, 24 hours, 26 hours, 28 hours, 30 hours, 32 hours, 34 hours, 36 hours, 38 hours, 40 hours, 42 hours, 44 hours, 46 hours, 48 hours, 50 hours, 52 hours, 54 hours, 56 hours, 58 hours, 60 hours, 62 hours, 64 hours, 66 hours, 68 hours, 70 hours, 72 hours, 74 hours, 76 hours, 78 hours, 80 hours, 82 hours, 84 hours, 86 hours, 88 hours, 90 hours, 92 hours, 94 hours, 96 hours, 98 hours, 100 hours, 102 hours, 104 hours, 106 hours, 108 hours, 110 hours, 112 hours, 114 hours, 116 hours, 118 hours, 120 hours, 122 hours, 124 hours, 126 hours, 128 hours, 130 hours, 132 hours, 134 hours, 136 hours, 138 hours, 140 hours, 142 hours, 144 hours, 146 hours, 148 hours, 150 hours, 152 hours, 154 hours, 156 hours, 158 hours, 160 hours, 162 hours, 164 hours, 166 hours, 168 hours, 170 hours, 172 hours, 174 hours, 176 hours, 178 hours, 180 hours, 182 hours, 184 hours, 186 hours, 188 hours, 190 hours, 192 hours, 194 hours, 196 hours, 198 hours, 200 hours, 202 hours, 204 hours, 206 hours, 208 hours, 210 hours, 212 hours, 214 hours, 216 hours, 218 hours, 220 hours, 222 hours, 224 hours, 226 hours, 228 hours, 230 hours, 232 hours, 234 hours, 236 hours, 238 hours, 240 hours, 242 hours, 244 hours, 246 hours, 248 hours, 250 hours, 252 hours, 254 hours, 256 hours, 258 hours, 260 hours, 262 hours, 264 hours, 266 hours, 268 hours, 270 hours, 272 hours, 274 hours, 276 hours, 278 hours, 280 hours, 282 hours, 284 hours, 286 hours, 288 hours, 290 hours, 292 hours, 294 hours, 296 hours, 298 hours, 300 hours, 302 hours, 304 hours, 306 hours, 308 hours, 310 hours, 312 hours, 314 hours, 316 hours, 318 hours, 320 hours, 322 hours, 324 hours, 326 hours, 328 hours, 330 hours, 332 hours, 334 hours, 336 hours, 338 hours, 340 hours, 342 hours, 344 hours, 346 hours, 348 hours, 350 hours, 352 hours, 354 hours, 356 hours, 358 hours, 360 hours, 362 hours, 364 hours, 366 hours, 368 hours, 370 hours, 372 hours, 374 hours, 376 hours, 378 hours, 380 hours, 382 hours, 384 hours, 386 hours, 388 hours, 390 hours, 392 hours, 394 hours, 396 hours, 398 hours, 400 hours, 402 hours, 404 hours, 406 hours, 408 hours, 410 hours, 412 hours, 414 hours, 416 hours, 418 hours, 420 hours, 422 hours, 424 hours, 426 hours, 428 hours, 430 hours, 432 hours, 434 hours, 436 hours, 438 hours, 440 hours, 442 hours, 444 hours, 446 hours, 448 hours, 450 hours, 452 hours, 454 hours, 456 hours, 458 hours, 460 hours, 462 hours, 464 hours, 466 hours, 468 hours, 470 hours, 472 hours, 474 hours, 476 hours, 478 hours, 480 hours, 482 hours, 484 hours, 486 hours, 488 hours, 490 hours, 492 hours, 494 hours, 496 hours, 498 hours, 500 hours, 502 hours, 504 hours, 506 hours, 508 hours, 510 hours, 512 hours, 514 hours, 516 hours, 518 hours, 520 hours, 522 hours, 524 hours, 526 hours, 528 hours, 530 hours, 532 hours, 534 hours, 536 hours, 538 hours, 540 hours, 542 hours, 544 hours, 546 hours, 548 hours, 550 hours, 552 hours, 554 hours, 556 hours, 558 hours, 560 hours, 562 hours, 564 hours, 566 hours, 568 hours, 570 hours, 572 hours, 574 hours, 576 hours, 578 hours, 580 hours, 582 hours, 584 hours, 586 hours, 588 hours, 590 hours, 592 hours, 594 hours, 596 hours, 598 hours, 600 hours, 602 hours, 604 hours, 606 hours, 608 hours, 610 hours, 612 hours, 614 hours, 616 hours, 618 hours, 620 hours, 622 hours, 624 hours, 626 hours, 628 hours, 630 hours, 632 hours, 634 hours, 636 hours, 638 hours, 640 hours, 642 hours, 644 hours, 646 hours, 648 hours, 650 hours, 652 hours, 654 hours, 656 hours, 658 hours, 660 hours, 662 hours, 664 hours, 666 hours, 668 hours, 670 hours, 672 hours, 674 hours, 676 hours, 678 hours, 680 hours, 682 hours, 684 hours, 686 hours, 688 hours, 690 hours, 692 hours, 694 hours, 696 hours, 698 hours, 700 hours, 702 hours, 704 hours, 706 hours, 708 hours, 710 hours, 712 hours, 714 hours, 716 hours, 718 hours, 720 hours, 722 hours, 724 hours, 726 hours, 728 hours, 730 hours, 732 hours, 734 hours, 736 hours, 738 hours, 740 hours, 742 hours, 744 hours, 746 hours, 748 hours, 750 hours, 752 hours, 754 hours, 756 hours, 758 hours, 760 hours, 762 hours, 764 hours, 766 hours, 768 hours, 770 hours, 772 hours, 774 hours, 776 hours, 778 hours, 780 hours, 782 hours, 784 hours, 786 hours, 788 hours, 790 hours, 792 hours, 794 hours, 796 hours, 798 hours, 800 hours, 802 hours, 804 hours, 806 hours, 808 hours, 810 hours, 812 hours, 814 hours, 816 hours, 818 hours, 820 hours, 822 hours, 824 hours, 826 hours, 828 hours, 830 hours, 832 hours, 834 hours, 836 hours, 838 hours, 840 hours, 842 hours, 844 hours, 846 hours, 848 hours, 850 hours, 852 hours, 854 hours, 856 hours, 858 hours, 860 hours, 862 hours, 864 hours, 866 hours, 868 hours, 870 hours, 872 hours, 874 hours, 876 hours, 878 hours, 880 hours, 882 hours, 884 hours, 886 hours, 888 hours, 890 hours, 892 hours, 894 hours, 896 hours, 898 hours, 900 hours, 902 hours, 904 hours, 906 hours, 908 hours, 910 hours, 912 hours, 914 hours, 916 hours, 918 hours, 920 hours, 922 hours, 924 hours, 926 hours, 928 hours, 930 hours, 932 hours, 934 hours, 936 hours, 938 hours, 940 hours, 942 hours, 944 hours, 946 hours, 948 hours, 950 hours, 952 hours, 954 hours, 956 hours, 958 hours, 960 hours, 962 hours, 964 hours, 966 hours, 968 hours, 970 hours, 972 hours, 974 hours, 976 hours, 978 hours, 980 hours, 982 hours, 984 hours, 986 hours, 988 hours, 990 hours, 992 hours, 994 hours, 996 hours, 998 hours, 1000 hours, 1002 hours, 1004 hours, 1006 hours, 1008 hours, 1010 hours, 1012 hours, 1014 hours, 1016 hours, 1018 hours, 1020 hours, 1022 hours, 1024 hours, 1026 hours, 1028 hours, 1030 hours, 1032 hours, 1034 hours, 1036 hours, 1038 hours, 1040 hours, 1042 hours, 1044 hours, 1046 hours, 1048 hours, 1050 hours, 1052 hours, 1054 hours, 1056 hours, 1058 hours, 1060 hours, 1062 hours, 1064 hours, 1066 hours, 1068 hours, 1070 hours, 1072 hours, 1074 hours, 1076 hours, 1078 hours, 1080 hours, 1082 hours, 1084 hours, 1086 hours, 1088 hours, 1090 hours, 1092 hours, 1094 hours, 1096 hours, 1098 hours, 1100 hours, 1102 hours, 1104 hours, 1106 hours, 1108 hours, 1110 hours, 1112 hours, 1114 hours, 1116 hours, 1118 hours, 1120 hours, 1122 hours, 1124 hours, 1126 hours, 1128 hours, 1130 hours, 1132 hours, 1134 hours, 1136 hours, 1138 hours, 1140 hours, 1142 hours, 1144 hours, 1146 hours, 1148 hours, 1150 hours, 1152 hours, 1154 hours, 1156 hours, 1158 hours, 1160 hours, 1162 hours, 1164 hours, 1166 hours, 1168 hours, 1170 hours, 1172 hours, 1174 hours, 1176 hours, 1178 hours, 1180 hours, 1182 hours, 1184 hours, 1186 hours, 1188 hours, 1190 hours, 1192 hours, 1194 hours, 1196 hours, 1198 hours, 1200 hours, 1202 hours, 1204 hours, 1206 hours, 1208 hours, 1210 hours, 1212 hours, 1214 hours, 1216 hours, 1218 hours, 1220 hours, 1222 hours, 1224 hours, 1226 hours, 1228 hours, 1230 hours, 1232 hours, 1234 hours, 1236 hours, 1238 hours, 1240 hours, 1242 hours, 1244 hours, 1246 hours, 1248 hours, 1250 hours, 1252 hours, 1254 hours, 1256 hours, 1258 hours, 1260 hours, 1262 hours, 1264 hours, 1266 hours, 1268 hours, 1270 hours, 1272 hours, 1274 hours, 1276 hours, 1278 hours, 1280 hours, 1282 hours, 1284 hours, 1286 hours, 1288 hours, 1290 hours, 1292 hours, 1294 hours, 1296 hours, 1298 hours, 1300 hours, 1302 hours, 1304 hours,